UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)(KMW)**

PLAINTIFFS' REPLY IN SUPPORT OF *DAUBERT* MOTION TO EXCLUDE TESTIMONY OF JOHN M. FLACK, M.D.

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I. INTRODUCTION

Defendants attempt to deflect from Dr. Flack's off-point qualifications and his deficient methodology, which resulted in Dr. Flack's failure to consider decades' worth of literature regarding NDMA/NDEA. Defendants' Opposition (Dkt. No. 1791 ("the Opposition")) is premised on the wrong question: whether valsartan *itself* causes cancer. (*See, e.g.*, Opp'n at 5 ("As an internal medicine physician specializing in hypertension, ***Dr. Flack is permitted to opine on whether the literature establishes an association between valsartan and cancer*** based on the literature review he performed." (emphasis added)).) The correct question – as Defendants well know – is whether valsartan contaminated with carcinogens NDMA/NDEA can cause cancer.

To the extent Dr. Flack evaluated whether valsartan *itself* causes cancer (apart from the NDMA/NDEA contamination), his opinions should be excluded as patently unhelpful to the jury and Court. Fed. R. Evid. 702(a) (requiring that the expert "help the trier of fact to understand the evidence or to determine a fact in issue"); *see also Schneider ex rel. Est. of Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003) (stating that "expert testimony must fit the issues in the case … [i]n other words, the expert's testimony must be relevant for the purposes of the case and must assist the trier of fact"). Dr. Flack's testimony would do nothing but waste time and serve to confuse the trier of fact as to what is at issue.

If Dr. Flack was attempting to answer the question actually presented in this ligation (*i.e.,* whether valsartan contaminated with NDMA/NDEA can cause cancer), the outcome is no better. Dr. Flack's opinions should be stricken on account of his off-point qualifications as to the general causation question presented in this litigation, his unreliable methodologies, and his retracted opinions.

II. ARGUMENT

A. Defendants' Opposition Admits Dr. Flack's Lack of Relevant Qualifications to the General Causation Inquiry

The general causation question in this litigation is whether NDMA/NDEA cause cancer. As a hypertension clinician, Dr. Flack's qualifications are entirely off-point.

Dr. Flack has never once in his professional career had occasion to: (1) study NDMA or NDEA or nitrosamines; (2) study the toxicological nature and/or the propensity of *any* chemical structure to cause cancer; or (3) study cancer at all. (*See* Dkt. No. 1706 ("Pls' Mot."), at 5.)

Defendants' Opposition actually underscores Dr. Flack's lack of pertinent qualifications:

> Defendants have offered Dr. Flack as an expert in hypertension. He is not offering toxicology or oncology opinions. His opinions center on hypertension and the relationship between hypertension and associated risk factors of cancer development. Dr. Flack is indisputably qualified to offer such opinions.

(Defs' Opp'n, at 8-9 (emphasis added).)

In making the above-quoted argument in the Opposition, Defendants strip away portions of Dr. Flack's Report and deposition testimony that go beyond shared risk factors present in some hypertension patients and cancer risk, and which appears Section V.O of Dr. Flack's Report. That discussion itself is simply not germane to *general* causation and should be excluded as well for that reason.

Sections VII, VIII, and IX of Dr. Flack's Report go far beyond a discussion of those supposedly shared risk factors. Section VIII of Dr. Flack's Report is titled "Medical and Scientific Literature Does Not Support a Causal Relationship Between Trace Amounts of NDMA/NDEA in Valsartan and Cancer Development." (Flack Rep., at 31 (Pls' Mot., Ex. 1.).) And then Section IX of Dr. Flack's Report continues the discussion of NDMA/NDEA and cancer causation by comparing such risk (from Section VIII) to the shared risk factors discussed in Section V.O. And

Dr. Flack even attempts to assert in Section VII of his Report that he did not witness any cancer cases among hypertension patients exposed to NDMA/NDEA in VCDs; he later admitted he did nothing to substantiate this assertion and then retracted this opinion at his deposition. (Flack Rep., at 30; Pls' Mot. at 13-16.)

By Defendants' own admission, Dr. Flack is unqualified to offer those opinions found in Sections VII, VIII, and IX of his Report. (Defs' Opp'n, at 8 ("He is not offering toxicology or oncology opinions.")). For this reason alone, the Court should exclude Dr. Flack's opinions in Sections VII, VIII, and IX of his Report (as well as any portions of his Report that rely on these sections).

B. Defendants Have Disavowed Offering Dr. Flack as an Epidemiology Expert, an Admission that is Fatal to Dr. Flack's Qualifications for the Opinions Offered in Sections VII, VIII and IX of his Report

Defendants state in their Opposition that "Dr. Flack … has been offered as a clinical expert, not as an epidemiology expert." (Opp'n, at 15 (emphasis added).) This means that all of Dr. Flack's opinions are being offered from his perspective as a *hypertension clinician*. In support of Dr. Flack, Defendants make the following assertions in the Opposition:

- "[Dr. Flack] is well-qualified given his decades of experience treating patients with hypertension in his clinical practice." (Opp'n, at 2.)
- "As a medical doctor, Dr. Flack regularly researches, reviews, and analyzes medical literature in his clinical practice … to form conclusions on the safety of drugs based on medical literature in treating his patients. He employed the same methodology here." (Opp'n, at 4.)
- "As an internal medicine physician specializing in hypertension, Dr. Flack is permitted to opine on whether the literature establishes an association between valsartan and cancer based on the literature review he performed." (Opp'n, at 5.)
- "**Defendants have offered Dr. Flack as an expert in hypertension**. **He is not offering toxicology or oncology opinions**. **His opinions center on hypertension and the relationship between hypertension and associated risk**

factors of cancer development." (Opp'n, at 8-9 (emphasis added).)

- "As a clinical physician specializing in the treatment of hypertensive patients, Dr. Flack is qualified to review and interpret medical literature pertaining to the drugs he regularly prescribes to opine on their safety." (Opp'n, at 14.)

Dr. Flack's qualifications only support his opinions up through Section VI of his Report, however (and which opinions do not pertain to general causation). Everything beyond Section VI is far beyond Dr. Flack's hypertension clinician's expertise, as Defendants themselves directly admit throughout the Opposition.

Despite the above, Defendants argue that Dr. Flack also opines that NDMA/NDEA present in Defendants' VCDs "do not independently cause, or increase the risk of, the types of cancer alleged" and that "[n]o medical professional could credibly claim that Plaintiffs' cancers are cause by their use of valsartan" contaminated with NDMA/NDEA. (Opp'n, at 17.). Sections VII, VIII, and IX of Dr. Flack's Report – which primarily address the cancer-causing potential of NDMA/NDEA – clearly go far beyond the expertise of a hypertension clinician, and beyond the scope of the opinions the defense argues to keep viable. Sections VII, VIII, and IX of Dr. Flack's Report and his opinions therein should be precluded.

C. Even If Dr. Flack Was Offered as an Epidemiology Expert, He Is Unqualified to Offer the Opinions in Sections VII, VIII, and IX of His Report

Even if Dr. Flack was basing the opinions in Sections VII, VIII and IX of his Report on his supposed epidemiology qualifications (which Defendants have disavowed, *supra*), his attempt to opine on topics he *admittedly* has never once studied would make it even more important that he conduct an extensive literature review, at least addressing the various categories of relevant scientific data, in order to qualify himself sufficiently to offer an epidemiology-based opinion on NDMA/NDEA and cancer causation. However, Dr. Flack's literature review does not even come close to meeting the grade; Dr. Flack omitted decades' worth of literature on NDMA/NDEA and

omitted entire categories of relevant scientific studies, as discussed herein. In short, Dr. Flack had no relevant knowledge or experience to rely on to answer the question at issue prior to becoming engaged as an expert witness, and he did not apply a reliable methodology to address the question once retained.

D. Dr. Flack's Unreliable Literature Search

Defendants do not dispute Plaintiffs' characterization of Dr. Flack's search in PubMed, which was for "'valsartan' ***and*** 'NDMA'" and thus would have only generated hits for literature containing both terms. (Defs' Opp'n, at 11.) Rather, Defendants pretend that this is a sufficient search to evaluate the carcinogenic potential of NDMA/NDEA as present in their VCDs. Defendants' own toxicologist employees freely admitted that NDMA/NDEA have been studied for nearly 150 years, and yet Dr. Flack's (and Defendants') myopic view is that all of that literature is to be discarded and ignored because it occurred outside the medium of valsartan. If Dr. Flack truly believes as much, it betrays a fundamental lack of understanding of the subject matter, and more importantly, a failure to apply a legally acceptable methodology.

In an effort to rehabilitate Dr. Flack, Defendants assert that he "obtained and reviewed" documents from other experts, from bibliographies of certain articles, and from materials he was provided by counsel, and that such efforts resulted in a "robust collection" of literature. (Defs' Opp'n, at 10-11 (citing Flack Rep., Ex. B ("Materials Considered").) Defendants' assertion that Dr. Flack "obtained *and reviewed*" the information in Exhibit B to his Report, is completely misrepresentative of Dr. Flack's testimony. ***To simply collect is not enough; one must actually read.*** And Dr. Flack admitted that he did not read much of what was provided to him. Dr. Flack testified the following way about how to regard his "Materials Considered" list found at Exhibit B:

> Everything that was supplied to me did not get extensively review [sic]. Some of it was cursorily reviewed, ***some of it was not reviewed. You simply have what was supplied to me***.

(Flack Dep. 58:6-9 (emphasis added).)

The result of this deficient search combined with Dr. Flack's cherry-picking among an already cherry-picked set of documents mostly provided to him by counsel is his omission of entire categories of literature regarding NDMA/NDEA and cancer.[1] These include specifically dietary studies and mechanistic studies studying the human carcinogenicity of NDMA/NDEA. Defendants attempt to explain this omission away by arguing that those "studies simply did not pertain to Dr. Flack's inquiry because they had nothing to do with NDMA or NDEA ***in valsartan***." (Defs' Opp'n, at 14 (emphasis added).) The fundamental problem is that Dr. Flack failed to actually review those categories of literature in order to reason to an opinion as to why they are significant, or not. On top of that, such an opinion flies in the face of the methodology leading to the scientific consensus that NDMA and NDEA are probable human carcinogens.

The lens through which Dr. Flack views the inquiry definitively establishes the unreliability of Dr. Flack's approach. Essentially, Defendants take the position that unless NDMA/NDEA was studied "in valsartan" the studies have no bearing on general causation in this case. There is zero legal or methodological support for such a proposition, and it is at odds with the approach of the numerous scientific bodies that have evaluated the carcinogenic potential of NDMA/NDEA including in Defendants' VCDs. All of those scientific bodies have used a full body of literature regarding NDMA/NDEA in their evaluations of its carcinogenicity including dietary and mechanistic studies.[2]

[1] Moreover, Dr. Flack fails to actually analyze and rely on another defense expert's report or opinions.
[2] A notable example is the WHO's 2002 Concise International Chemical Assessment Document 38 of NDMA and NDEA, which for NDMA is attached hereto as **Exhibit 1**.

In short, Dr. Flack did not conduct a "reliable literature review" by obtaining a fulsome "snapshot" of the existing literature that bears on the topic; rather, he has limited himself to a couple of pixels. *In re Lipitor*, 174 F. Supp. 3d at 929 (quoting *In re Zimmer Nexgen Knee Implant Prods. Liab. Litig.*, No. 11cv5468, 2015 WL 5050214, at *3 (N.D. Ill. Aug. 25, 2015) (attached hereto as **Ex. 5**)). Plaintiffs do not focus on the failure to look at all studies in each category, rather it is the failure to consider any studies in one or more categories. As Dr. Flack himself conceded, this cherry-picked approach would be "blasted" in academia. (Flack Dep. 121:6-122:22 (emphasis added).) *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 242 (S.D.N.Y. 2018) ("'[A]n expert may not 'pick and choose' from the scientific landscape and present the Court with what he believes the final picture looks like.' Where an expert ignores evidence that is highly relevant to his [or her] conclusion, contrary to his [or her] own stated methodology, exclusion of the expert's testimony is warranted.").

E. Dr. Flack Failed to Conduct a Weight of the Evidence/Bradford Hill Analysis

Defendants' position appears to be that Dr. Flack was not required to conduct a weight of the evidence or Bradford Hill analysis because he was not being offered as an epidemiology expert. (Opp'n, at 15.) The Court should value substance over labels. Section VIII, in particular, of Dr. Flack's Report presents as an epidemiological literature review and plainly includes the opinion that NDMA/NDEA do not cause cancer. Dr. Flack's discussion of carcinogenicity in Section VIII (which is used in Section IX also) is legally and methodologically deficient, as are Dr. Flack's off-point qualifications. Dr. Flack clearly did not examine any Bradford Hill criteria; he also cannot claim to have done a weight of the evidence analysis since he never asserted as much in his Report or deposition, and because such an analysis actually requires reviewing the evidence.

F. Defendants Agree with Dr. Flack's Clarification of Section VII of His Report

Section VII of Dr. Flack's Report asserted that he "did not witness any patients have an adverse effect as a result of the NDMA/NDEA impurities found in valsartan." (Flack Rep., at 30.) Although the sentence on its face would appear to make the assertion that Dr. Flack was referring to cancer diagnoses as a result of NDMA/NDEA exposure, Dr. Flack clarified in his deposition that he only meant that switching to alternative therapies was not an issue and that the statement had nothing to do with cancer outcomes. (*See* Pls' Mot., at 13-16 (block quoting Dr. Flack's testimony with deposition citations).). As clarified, this opinion does not address general causation, and actually supports Plaintiffs' position that numerous safer alternatives to Defendants' contaminated VCDs existed at all relevant times.

Prior to filing the Motion and after Dr. Flack's deposition, Plaintiffs had sought a stipulation from Defendants that Dr. Flack was not opining that: (1) that he did not witness cancer diagnoses as a result of NDMA/NDEA exposure among his patients; and (2) that he ruled out NDMA/NDEA exposure as a cause of cancer diagnoses among his patients. (**Ex. 2** (J. Davis S. Fowler 10/11/21 Email).) The stipulation was consistent with Dr. Flack's deposition testimony that he was "not talking about cancer." (Pls.' Mot. 13-16.) Defendants refused the proposed stipulation. (Id.) As a result, Plaintiffs submitted the Motion which included the section regarding Dr. Flack's retracted opinion. (*See* Pls' Mot., at 13-16.)

Yet, Defendants have now essentially so stipulated, as they have agreed with the characterization that Dr. Flack "does not mean cancer" with his use of the term "adverse effect" in Section VII of his Report and instead means ability to quickly find alternative therapies.[3]

[3] Plaintiffs should be entitled to costs for being forced to brief this issue when a clear and simple stipulation was proposed, rejected, and then now conceded to by Defendants only after briefing.

(Opp'n, at 19.) Thus, Dr. Flack's opinion (as clarified) that patients had no issues switching to alternative therapies does not pertain to general causation and should be stricken.[4]

III. CONCLUSION

In sum, Dr. Flack is being offered by Defendants as a hypertension clinician, and he has no relevant qualifications to opine regarding the propensity of NDMA/NDEA to cause cancer. And even if he was qualified, Dr. Flack's deficient methodology that omitted decades' worth and entire categories of relevant evidence should result in his disqualification. Finally, Dr. Flack's remaining opinions that do match up his qualifications simply are not germane to the general causation inquiry. For the foregoing reasons, Dr. Flack should be excluded from offering any opinions related to general causation.

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Respectfully submitted,

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[4] In addition, the sentence at issue in Section VII of Dr. Flack's Report has a tendency to mislead and cause confusion as to Dr. Flack's opinion stated therein, and should be ordered stricken for that reason as well.

CERTIFICATE OF SERVICE

I hereby certify that on January 6, 2022, I electronically filed a redacted version the foregoing document with the Clerk of the Court using the CM/ECF system which will send notifications of such filing to the CM/ECF participants registered to receive service in this MDL. In addition, I hereby certify that unredacted copies of foregoing document will be served contemporaneous to filing via email on the Court, Special Master, and the Defense Executive Committee at DECValsartan@btlaw.com.

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